

## **REMARKS**

### **Status of the Claims**

Claims 2, 52-96, 99-101, 103-106 and 112 are all the claims pending in the application. Claims 52-56, 59-62, 65-67, 69-71, 73, 74 and 104-106 are withdrawn from consideration as being directed to nonelected inventions. Claims 1, 3-51, 97-98, 102, and 107-111 are canceled.

Claims 2, 75-77, 79, 82-85, 88-90, 93, 94, 100, 103 and 112 are rejected. Claims 57, 58, 63, 64, 68, 72, 78, 80, 81, 86, 87, 91, 92, 95, 96, 99 and 101 are objected to.

### **Information Disclosure Statement**

Applicants thank the Examiner for acknowledgement of the Information Disclosure Statement filed August 17, 2007, by returning a signed and initialed copy of the PTO Form SB/08 submitted therewith.

### **Restriction and Species Election**

On page 2 of the Office Action, the Examiner acknowledges Applicants' election of Group III, directed to compounds of Formula I wherein Q is formula IV (pyrimidine), and pharmaceutical compositions thereof. The Examiner also acknowledges Applicant's species election of the compound disclosed in Example 3398, namely 3-chloro-N-[cis-4-(4-dimethylamino-5-methyl-pyrimidin-2-ylamino)-cyclohexyl]-4-fluorobenzamide methane-sulfonic acid.

The Examiner asserts that Claims 2, 57, 58, 63, 64, 68, 72, 75-101, 103 and 112 read on the elected species, and these claims are under examination only to the extent that they are patentably indistinct from the elected species. The Examiner asserts that claims 52-56, 59-62, 65-67, 69-71, 73, 74 and 104-106 remain withdrawn as being directed towards non-elected species. The Examiner has acknowledged Applicants' request for rejoinder of method claims

104-106, and asserts that these claims shall be held in abeyance pending determination of the allowability of the compound and compositions claims.

In addition, Applicants respectfully request that should the claims that read on the elected species be found patentable, the Examiner is respectfully requested to perform additional searching to determine the patentability of additional non-elected species within those claims that read on elected Group III, namely Claims 2, 52-96, 99-101 and 103.

**Response To Rejection Under 35 U.S.C. § 103**

On page 3 of the Office Action, the Office Action rejects Claims 2, 75-77, 79, 82-85, 88-90, 93, 94, 100, 103 and 112 under 35 U.S.C. §103(a) as being obvious over Wustrow et al. ( J. Med. Chem. 41(5):760-771; “Wustrow”). The Office Action asserts that the instant claims are rendered obvious by the following compounds disclosed by Wustrow:

1. RN 204245-70-5, 2-Pyrimidinamine, N-[4-[2-[methyl(phenylmethyl)amino]ethyl]cyclohexyl]-, trans-,
2. RN 204245-89-6, 2-Pyrimidinamine, N-[4-[2-(dipropylamino)ethyl]cyclohexyl]-, trans-,
3. RN 189153-07-9, Cyclohexanecarboxylic acid, 4-(2-pyrimidinylamino)-, ethyl ester, trans-,

The Office Action alleges that the above compounds are homologs of the presently claimed compounds, because the above-compounds contain hydrogen as the R<sub>2</sub> group, whereas the instant claims mandate the the compound always has a substituent as the R<sub>2</sub> group.

The Office Action alleges that it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the compounds disclosed by Wustrow in order to generate alkyl homologs and position isomers thereof. The Office Action asserts that one of

ordinary skill in the art would have been motivated to generate the instantly claimed compounds because these structural homologs and isomeric compounds would also be expected to exhibit high affinity for serotonin and dopamine receptors. To support this position, the Office Action asserts that it has been held that structurally homologous or isomeric compounds are *prima facie* obvious, absent a showing of unexpected results.

Initially, Applicants note that the Office Action appears to suggest that the compounds disclosed by Wustrow are homologs, or isomers, of the instantly claimed compounds. However, according to M.P.E.P. § 2144.09, and as admitted by the Office Action, homologs are defined as compounds which “[differ] regularly by the successive addition of the same chemical group” and isomers are defined as “compounds having the same radicals in physically different positions on the same nucleus.” According to these definitions, the compounds disclosed by Wustrow cannot reasonably be considered true homologs. In particular, compound (3) as noted above (i.e., RN 189153-07-9) has marked structural differences at several positions that precludes its classification as a homolog. Specifically, (a) the group corresponding to group L of instant formula (I) is distinct from that recited in the instant claims, (b) the R1 group of compound (3) is an ethoxy group, which is not a substituent encompassed by the instant claims, and (c) the R2 group is invariantly hydrogen, whereas the instant compounds always have a substituent as the R2 group. Further, compound (3) of Wustrow et al. is not sufficiently similar to the claimed compound such that one of ordinary skill in the art would be motivated to make the claimed compounds. Further still, with specific regard to compound (3), and pursuant to M.P.E.P. § 2144.09, “if the prior art does not teach any specific or significant utility for the disclosed compounds, then the prior art is not sufficient to render structurally similar claims *prima facie* obvious because there is no motivation for one of ordinary skill in the art to make the reference

compounds, much less any structurally related compounds.” In this regard, compound (3) is an intermediate compound in the production of final tertiary amine compounds. Thus, Wustrow fails to disclose any specific or significant utility for the intermediate compound (3). One of ordinary skill in the art would not have been motivated to make the claimed compounds.

However, even if one of ordinary skill in the art were motivated to modify compound (3), which is not the case, there is no suggestion within the references, or from the Office Action, why it would be obvious to terminate the reaction at this step.

With specific regard to compounds (1) and (2) (i.e., RN 204245-70-5 and RN 204245-89-6), these compounds and the claimed compounds are different at the  $R_2$  group. Specifically, the instant compounds all contain a substituent as the  $R_2$  group, whereas in the compounds disclosed by Wustrow, the  $R_2$  group is invariantly hydrogen.

The claimed compounds are different from compounds (1) and (2) of Wustrow for at least the following reasons:

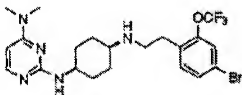
(a) The claimed compounds contain a substituent such as halogen, hydroxyl, carboxy, etc., as the  $R_2$  group. In contrast, the group corresponding to  $R_2$  in compounds (1) and (2) of Wustrow is invariably hydrogen.

(b) The configuration concerning the central cyclohexane ring of moiety L of the claimed compounds (1, 4-*cis*-cyclohexyl) differs from that of compounds (1) and (2) of Wustrow (1,4-*trans*-cyclohexyl).

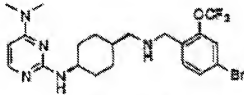
Therefore, compounds (1) and (2) of Wustrow are not true homologs.

Furthermore, as demonstrated in the Rule 1.132 Declaration by Mr. Kanuma submitted herewith, compounds (1) and (2) of Wustrow do not show any significant antagonist activity at human MCH1 receptors at a concentration of  $10\mu\text{M}$  ( $\text{IC}_{50} > 10\mu\text{M}$ ). In contrast, the claimed

compounds demonstrate remarkable and unexpectedly superior antagonist activity toward human MCH1 receptors. See the columns of “class” in the tables on pages 373-483, 518-519, 596-610 and 779-784, as well as the description on pages 796-803 of the specification, the definition of “class” being found on pages 798-9. In particular, the compounds of Examples 18 and 19, which are structurally most closely related to compounds (1) and (2) of Wustrow, show antagonist activity toward human MCH1 receptors, i.e., an  $IC_{50}$  of less than 50nM. See Table on page 799 of the specification. The claimed compounds show antagonist activity toward human MCH1 receptors that is unexpectedly superior in comparison to compounds (1) and (2) of Wustrow.



**Example 18**  
 $IC_{50} < 50$  nM (Class1)



**Example 19**  
 $IC_{50} = 21$  nM (Class1)

Thus, the claimed compounds would not have been obvious to one of ordinary skill in the art, and one of ordinary skill in the art would not have been motivated to make the claimed compounds based upon the disclosure of Wustrow.

Accordingly, reconsideration and withdrawal of the rejection under §103(a) is respectfully requested.

#### **Response To Objections To The Claims**

On page 5 of the Office Action, the Office Action objects to Claims 57, 58, 63, 64, 68, 72, 78, 80, 81, 86, 87, 91, 92, 95, 96, 99 and 101 as dependent upon a rejected base claim.

However, the Office Action indicates that these claims would be allowable if rewritten in independent form including all limitations of the base claim and any intervening claims.

Applicants request, respectfully, that should the obviousness rejection be overcome, the Examiner examine the additional species that fall within Claims 52-101 as these claims contain elected Group III subject matter.

### **Conclusion**

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

/Tu A. Phan/

---

Tu A. Phan, Ph.D.  
Registration No. 59,392

SUGHRUE MION, PLLC  
Telephone: (202) 293-7060  
Facsimile: (202) 293-7860

WASHINGTON OFFICE

**23373**

CUSTOMER NUMBER

Date: April 8, 2008